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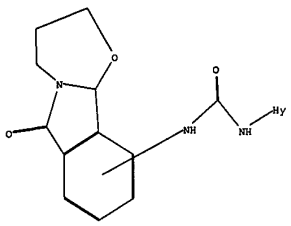

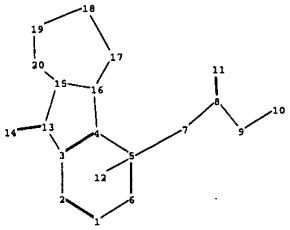

chain nodes :
7 8 9 10 11 14
ring nodes :
1 2 3 4 5 6 13 15 16 17 18 19 20
chain bonds :
7-8 8-9 8-11 9-10 13-14
ring bonds :
1-2 1-6 2-3 3-4 3-13 4-5 4-16 5-6 13-15 15-16 15-20 16-17 17-18 18-19 19-20
exact/norm bonds :
3-13 4-16 7-8 8-9 8-11 9-10 13-14 13-15 15-16 15-20 16-17 17-18 18-19 19-20
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom
11:CLASS 12:CLASS 13:Atom 14:CLASS 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom

L Number	Hits	Search Text	DB	Time stamp
1	374	544/101, 514/230.2	USPAT	2003/09/20 11:25
2	23533	kinase	USPAT	2003/09/20 11:25
3	7	(544/101, 514/230.2) and kinase	USPAT	2003/09/20 11:26

```
  * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 10:33:26 ON 20 SEP 2003

=> file reg
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'REGISTRY' ENTERED AT 10:33:34 ON 20 SEP 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   18 SEP 2003  HIGHEST RN 588668-76-2
DICTIONARY FILE UPDATES:  18 SEP 2003  HIGHEST RN 588668-76-2

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 10031795.str

L1      STRUCTURE UPLOADED

=> s l1
SAMPLE SEARCH INITIATED 10:33:51 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      5 TO ITERATE

100.0% PROCESSED       5 ITERATIONS                              1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            5 TO      234
PROJECTED ANSWERS:               1 TO       80

L2            1 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 10:34:00 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    133 TO ITERATE

100.0% PROCESSED     133 ITERATIONS                            18 ANSWERS
SEARCH TIME: 00.00.01
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L3 18 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY 148.15 TOTAL SESSION 148.36

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 10:34:05 ON 20 SEP 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 20 Sep 2003 VOL 139 ISS 13
FILE LAST UPDATED: 19 Sep 2003 (20030919/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

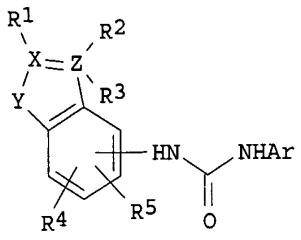
=> s l3
L4 2 L3

=> d ibib abs hitstr tot

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:591913 CAPLUS
DOCUMENT NUMBER: 137:150215
TITLE: Cdk4 and/or Cdk6 inhibitors with biaryl ureas and their salts as antitumor agents
INVENTOR(S): Hatayama, Satoshi; Hayashi, Kyoko; Honma, Mitsuki; Takahashi, Ikuko
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 194 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002220338	A2	20020809	JP 2001-18755	20010126

PRIORITY APPLN. INFO.: JP 2001-18755 20010126
OTHER SOURCE(S): MARPAT 137:150215
GI



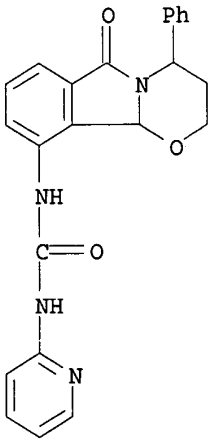
I

AB This invention relates to the general structures (I; Ar = N-contg. hetero arom. ring, X, Z = C, etc.; Y = CO, etc.; R1-R5 = H, etc.) and their salts as Cdk4 and/or Cdk6 inhibitors. I have antiproliferative effects on cancer cells and are potential antitumor agents. Formulation examples of I capsules, tablets, and injections were given.

IT **322687-73-0 322687-74-1 322687-92-3**
322688-08-4 322688-09-5 322688-26-6
322688-34-6 322688-35-7 322690-03-9
445431-59-4 445431-64-1 445431-68-5
445432-09-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Cdk4 and/or Cdk6 inhibitors with biaryl ureas and their salts as antitumor agents)

RN 322687-73-0 CAPLUS

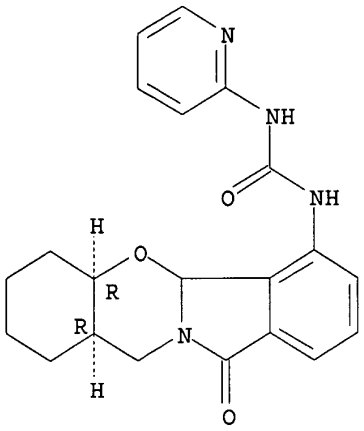
CN Urea, N-2-pyridinyl-N'-(3,4,6,10b-tetrahydro-6-oxo-4-phenyl-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)



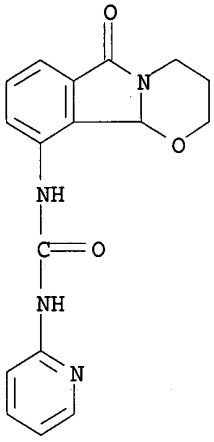
RN 322687-74-1 CAPLUS

CN Urea, N-[(5aR,9aR)-4b,5a,6,8,9,9a,10,12-octahydro-12-oxo-7H-isoindolo[1,2-b][1,3]benzoxazin-4-yl]-N'-2-pyridinyl- (9CI) (CA INDEX NAME)

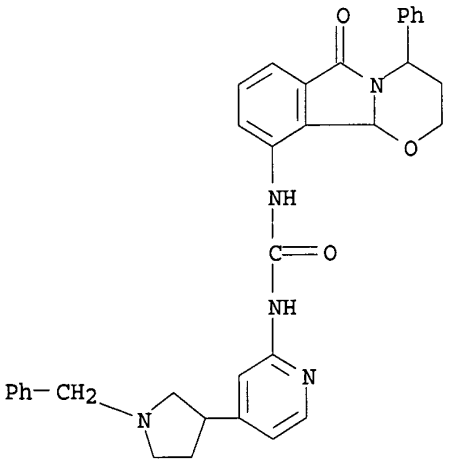
Absolute stereochemistry.



RN 322687-92-3 CAPLUS
CN Urea, N-2-pyridinyl-N'-(3,4,6,10b-tetrahydro-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)

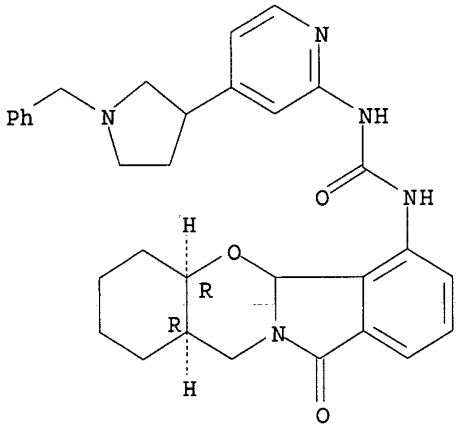


RN 322688-08-4 CAPLUS
CN Urea, N-[4-[1-(phenylmethyl)-3-pyrrolidinyl]-2-pyridinyl]-N'-(3,4,6,10b-tetrahydro-6-oxo-4-phenyl-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)

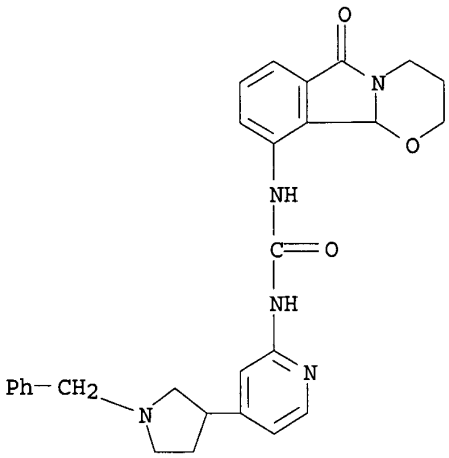


RN 322688-09-5 CAPLUS
CN Urea, N-[(5aR,9aR)-4b,5a,6,8,9,9a,10,12-octahydro-12-oxo-7H-isoindolo[1,2-b][1,3]benzoxazin-4-yl]-N'-[4-[1-(phenylmethyl)-3-pyrrolidinyl]-2-pyridinyl]- (9CI) (CA INDEX NAME)

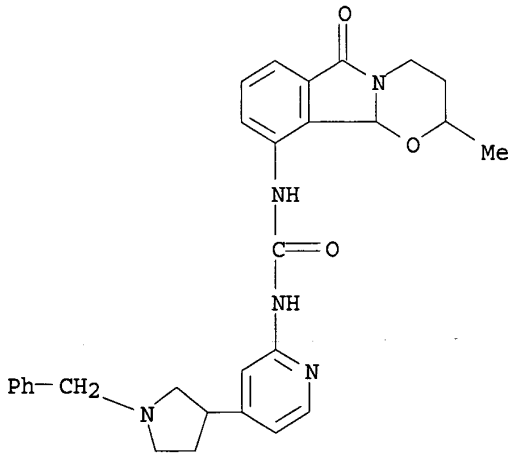
Absolute stereochemistry.



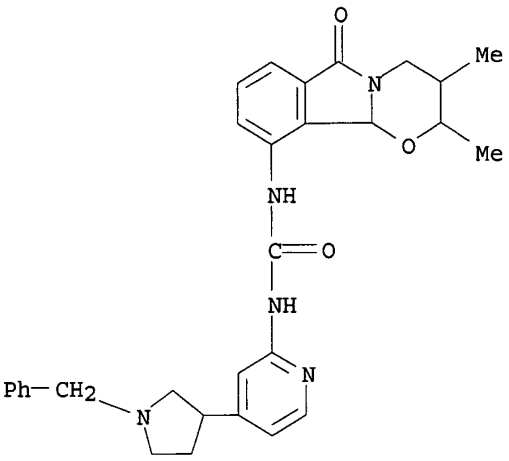
RN 322688-26-6 CAPLUS
CN Urea, N-[4-[1-(phenylmethyl)-3-pyrrolidinyl]-2-pyridinyl]-N'-(3,4,6,10b-tetrahydro-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)



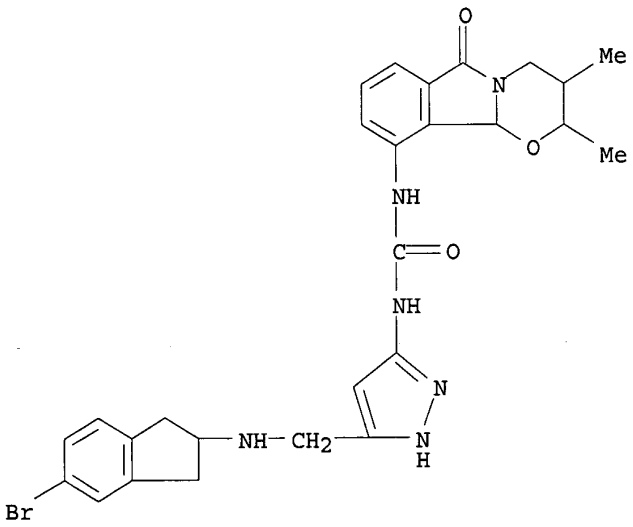
RN 322688-34-6 CAPLUS
CN Urea, N-[4-[1-(phenylmethyl)-3-pyrrolidinyl]-2-pyridinyl]-N'-(3,4,6,10b-tetrahydro-2-methyl-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)



RN 322688-35-7 CAPLUS
CN Urea, N-[4-[1-(phenylmethyl)-3-pyrrolidinyl]-2-pyridinyl]-N'-(3,4,6,10b-tetrahydro-2,3-dimethyl-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)

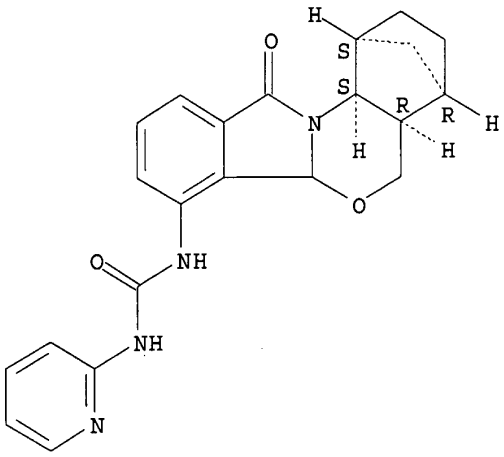


RN 322690-03-9 CAPLUS
CN Urea, N-[5-[[(5-bromo-2,3-dihydro-1H-inden-2-yl)amino]methyl]-1H-pyrazol-3-yl]-N'-(3,4,6,10b-tetrahydro-2,3-dimethyl-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)



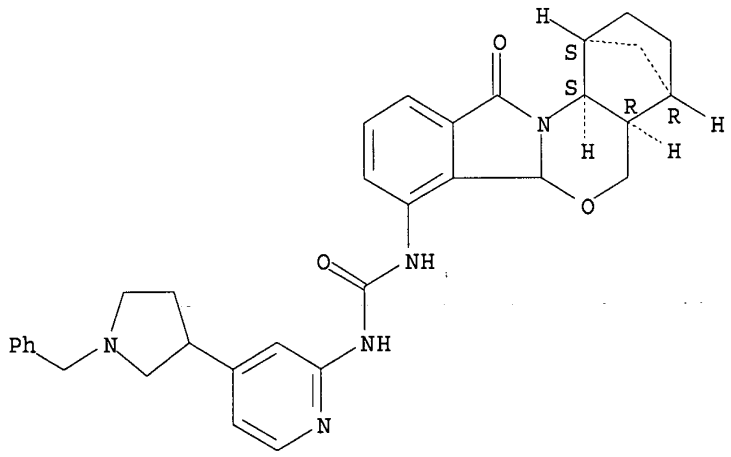
RN 445431-59-4 CAPLUS
CN Urea, N-[(1S,4R,4aR,12aS)-1,3,4,4a,5,6a,11,12a-octahydro-11-oxo-1,4-methano-2H-isoindolo[2,1-a][3,1]benzoxazin-7-yl]-N'-2-pyridinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

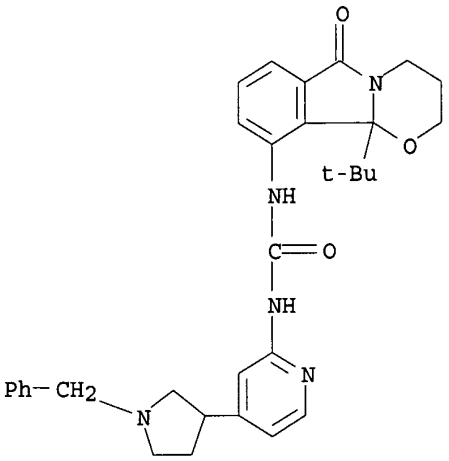


RN 445431-64-1 CAPLUS
CN Urea, N-[(1S,4R,4aR,12aS)-1,3,4,4a,5,6a,11,12a-octahydro-11-oxo-1,4-methano-2H-isoindolo[2,1-a][3,1]benzoxazin-7-yl]-N'-[4-[1-(phenylmethyl)-3-pyrrolidinyl]-2-pyridinyl]- (9CI) (CA INDEX NAME)

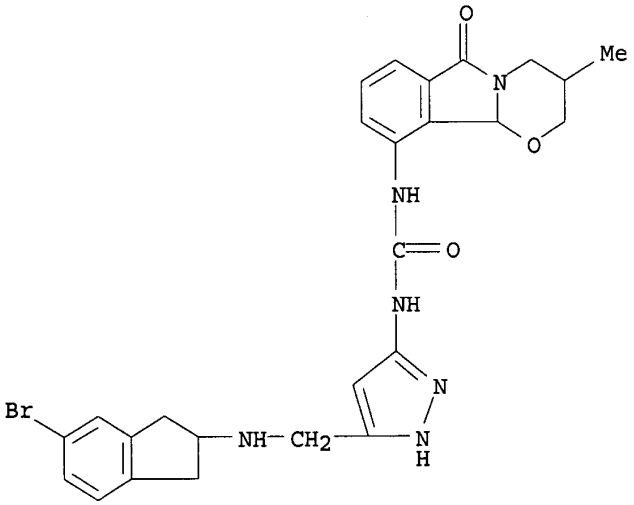
Absolute stereochemistry.



RN 445431-68-5 CAPLUS
CN Urea, N-[10b-(1,1-dimethylethyl)-3,4,6,10b-tetrahydro-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl]-N'-[4-[1-(phenylmethyl)-3-pyrrolidinyl]-2-pyridinyl]- (9CI) (CA INDEX NAME)



RN 445432-09-7 CAPLUS
CN Urea, N-[5-[[(5-bromo-2,3-dihydro-1H-inden-2-yl)amino]methyl]-1H-pyrazol-3-yl]-N'-(3,4,6,10b-tetrahydro-3-methyl-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)



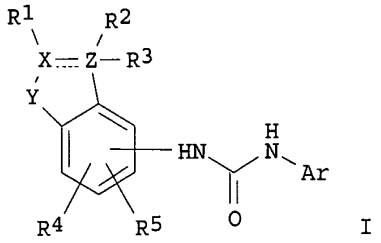
L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:78363 CAPLUS
DOCUMENT NUMBER: 134:147614
TITLE: Preparation of N,N'-biarylurea derivatives as inhibitors of cyclin-dependent kinases (Cdk4 and Cdk6)
INVENTOR(S): Hayama, Takashi; Hayashi, Kyoko; Honma, Mitsutaka; Takahashi, Ikuko
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 460 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

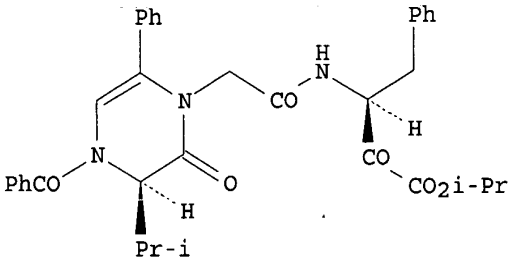
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001007411	A1	20010201	WO 2000-JP4991	20000726
W: AE, AG, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 2001106673	A2	20010417	JP 2000-274175	20000726
EP 1199306	A1	20020424	EP 2000-949909	20000726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: JP 1999-211384 A 19990726
WO 2000-JP4991 W 20000726

OTHER SOURCE(S): MARPAT 134:147614
GI



I



II

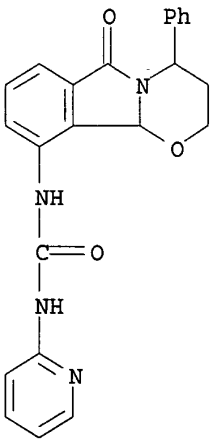
AB N-(hetero)aryl-N'-heterocyclylurea derivs. represented by general formula (I) [wherein Ar represents a nitrogenous heterocyclic arom. group such as (un)substituted pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, pyrazolyl, pyrrolyl, imidazolyl, indolyl, isoindolyl, quinolyl, isoquinolyl, benzothiazolyl, or benzoxazolyl; X and Z each represents C or N or together with R1 or R2 and/or R3 represent CH or N; Y represents CO, SO, or SO2; R1 represents hydrogen, (un)substituted lower alkyl, Y3-W2-Y4-R5, etc.; wherein R5 = H, (un)substituted lower alkyl, lower alkenyl, lower alkynyl, lower

cycloalkyl, aryl, imidazolyl, isoxazolyl, isoquinolyl, isoindolyl, indazolyl, indolyl, indolidinyl, isothiazolyl, ethylenedioxyphenyl, oxazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, pyrazolyl, quinoxalinyl, quinolyl, etc.; W2 = ingle bond, O, S, SO, SO2, N-(un)substituted NH, SO2NH, NHSO2NH, NHSO2, CONH, NHCO, NHCONH, NHCO2, etc.; Y3, Y4 = single bond, linear or branched lower alkylene; R2 and R3 each represents hydrogen, lower alkyl or alkoxy, or Y3-W2-Y4-R5 (Y3, W2, Y4, R5 = same as above), or one of R2 and R3 together with R1 and X forms cyclohexane, cyclopentane, piperidine, 3,4,5,6-tetrahydro-1,3-oxazine, tetrahydrothiopyran, pyrrolidine, tetrahydrothiofuran, oxazolidine ring, etc.; R4 and R5 represent H, halo, OH, amino, or Y3-W2-Y4-R5 (Y3, W2, Y4, R5 = same as above)] or salts thereof are prepd. The compds. (e.g. II) have a remarkable proliferation-inhibitory effect on tumor cells. A Cdk4 and/or Cdk6 inhibitor for use in the therapy of malignant tumor can hence be provided. II showed IC50 of 0.061 and 0.019 .mu.M against cyclin-D1-Cdk4 and cyclin-D2-Cdk4, resp., vs. 0.36 and 0.056 .mu.M, resp., for (.+-.)-flavopiridol, and inhibited the proliferation of HCT116 and MKN-1 cells with IC50 of 0.013 and 0.10 .mu.M, resp., vs. 0.15 and 0.87 .mu.M, resp., for (.+-.)-flavopiridol. Pharmaceutical formulations contg. I were prepd.

IT **322687-73-0P 322687-74-1P 322687-75-2P**
322687-92-3P 322688-08-4P 322688-09-5P
322688-10-8P 322688-26-6P 322688-28-8P
322688-29-9P 322688-34-6P 322688-35-7P
322690-03-9P 322690-04-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-(hetero)aryl-N'-heterocyclylurea derivs. as in inhibitors of cyclin-dependent kinases (Cdk4 and Cdk6) and antitumor agents)

RN 322687-73-0 CAPLUS

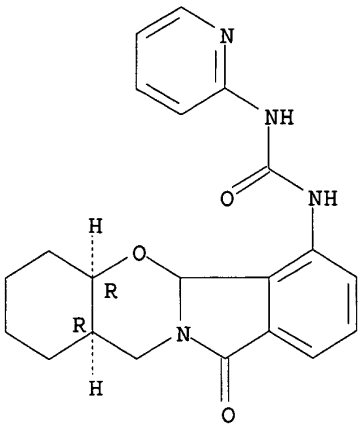
CN Urea, N-2-pyridinyl-N'-(3,4,6,10b-tetrahydro-6-oxo-4-phenyl-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)



RN 322687-74-1 CAPLUS

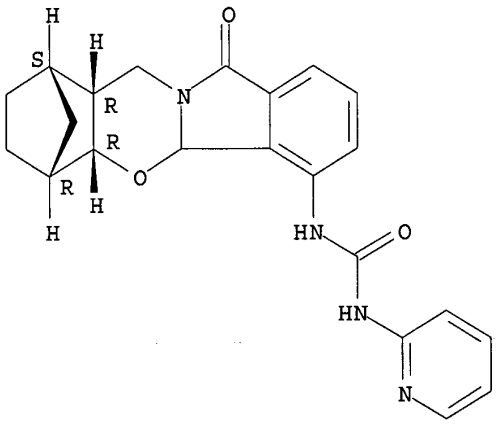
CN Urea, N-[(5aR,9aR)-4b,5a,6,8,9,9a,10,12-octahydro-12-oxo-7H-isoindolo[1,2-b][1,3]benzoxazin-4-yl]-N'-2-pyridinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

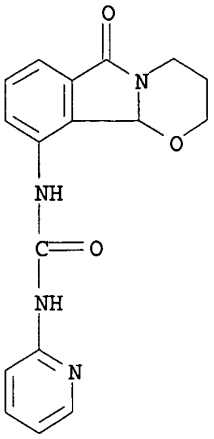


RN 322687-75-2 CAPLUS
CN Urea, N-[(5aR,6R,9S,9aR)-4b,5a,6,8,9,9a,10,12-octahydro-12-oxo-6,9-methano-7H-isoindolo[1,2-b][1,3]benzoxazin-4-yl]-N'-2-pyridinyl- (9CI) (CA INDEX NAME)

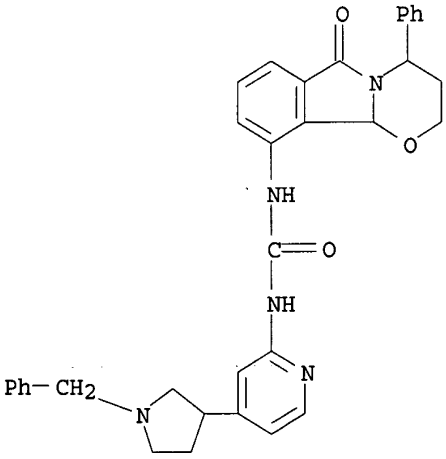
Absolute stereochemistry.



RN 322687-92-3 CAPLUS
CN Urea, N-2-pyridinyl-N'-(3,4,6,10b-tetrahydro-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)

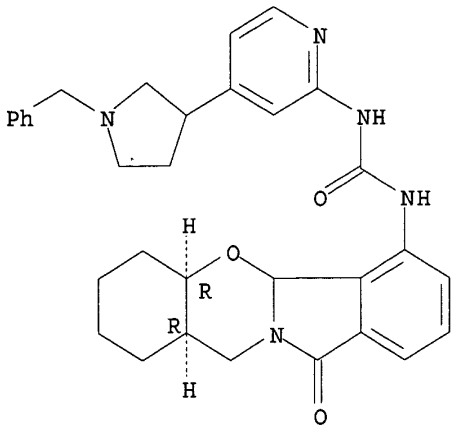


RN 322688-08-4 CAPLUS
CN Urea, N-[4-[1-(phenylmethyl)-3-pyrrolidinyl]-2-pyridinyl]-N'-(3,4,6,10b-tetrahydro-6-oxo-4-phenyl-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)



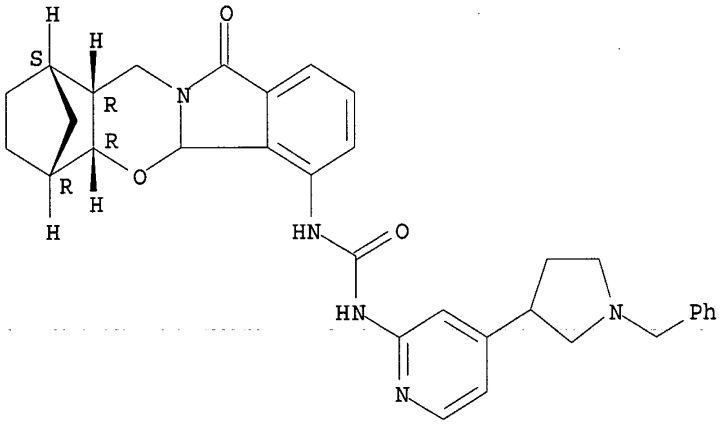
RN 322688-09-5 CAPLUS
CN Urea, N-[(5aR,9aR)-4b,5a,6,8,9,9a,10,12-octahydro-12-oxo-7H-isoindolo[1,2-b][1,3]benzoxazin-4-yl]-N'-[4-[1-(phenylmethyl)-3-pyrrolidinyl]-2-pyridinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

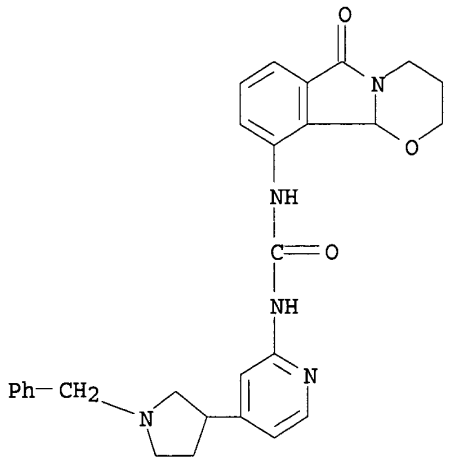


RN 322688-10-8 CAPLUS
CN Urea, N-[(5aR,6R,9S,9aR)-4b,5a,6,8,9,9a,10,12-octahydro-12-oxo-6,9-methano-7H-isoindolo[1,2-b][1,3]benzoxazin-4-yl]-N'-[3-[1-(phenylmethyl)-3-pyrrolidinyl]-2-pyridinyl]- (9CI) (CA INDEX NAME)

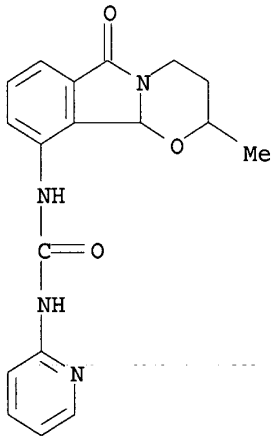
Absolute stereochemistry.



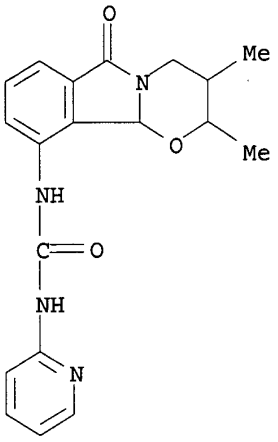
RN 322688-26-6 CAPLUS
CN Urea, N-[4-[1-(phenylmethyl)-3-pyrrolidinyl]-2-pyridinyl]-N'-(3,4,6,10b-tetrahydro-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)



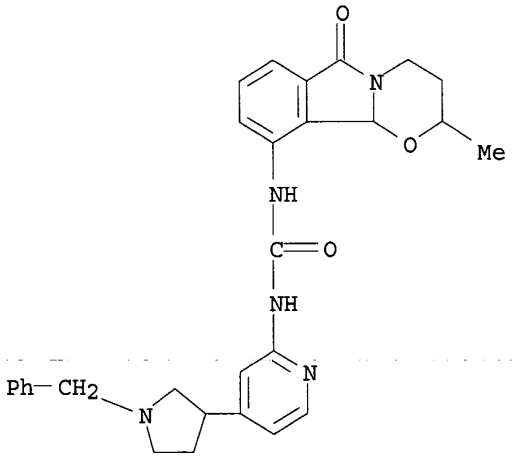
RN 322688-28-8 CAPLUS
CN Urea, N-2-pyridinyl-N'-(3,4,6,10b-tetrahydro-2-methyl-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)



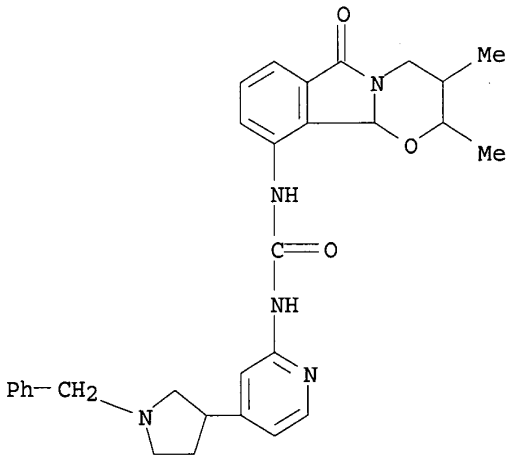
RN 322688-29-9 CAPLUS
CN Urea, N-2-pyridinyl-N'-(3,4,6,10b-tetrahydro-2,3-dimethyl-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)



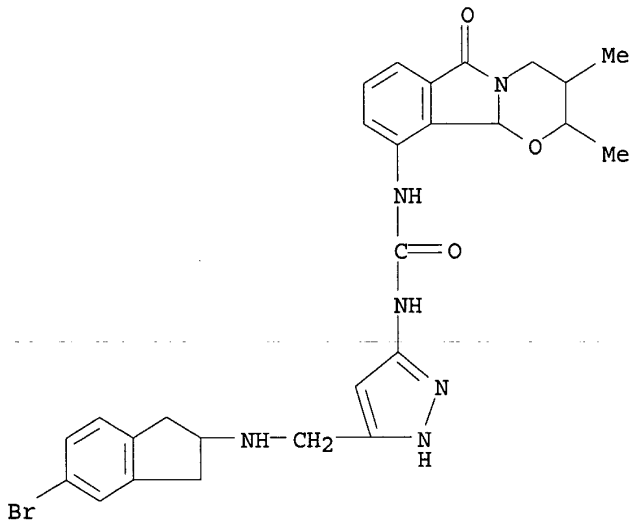
RN 322688-34-6 CAPLUS
CN Urea, N-[4-[1-(phenylmethyl)-3-pyrrolidinyl]-2-pyridinyl]-N'-(3,4,6,10b-tetrahydro-2-methyl-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)



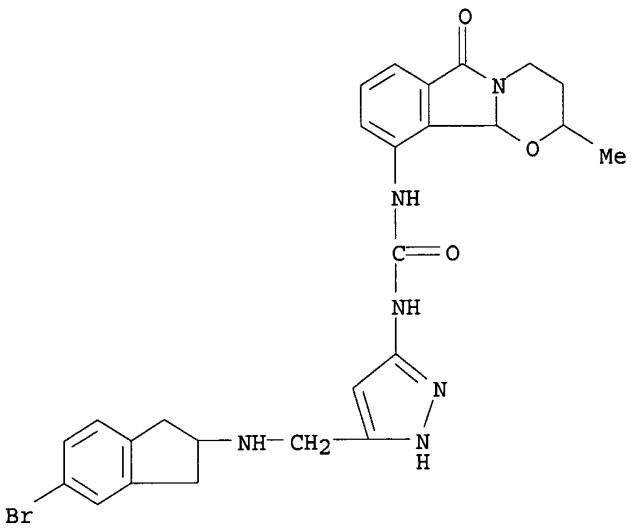
RN 322688-35-7 CAPLUS
CN Urea, N-[4-[1-(phenylmethyl)-3-pyrrolidinyl]-2-pyridinyl]-N'-(3,4,6,10b-tetrahydro-2,3-dimethyl-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)



RN 322690-03-9 CAPLUS
CN Urea, N-[5-[[(5-bromo-2,3-dihydro-1H-inden-2-yl)amino]methyl]-1H-pyrazol-3-yl]-N'-(3,4,6,10b-tetrahydro-2,3-dimethyl-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)



RN 322690-04-0 CAPLUS
CN Urea, N-[5-[[(5-bromo-2,3-dihydro-1H-inden-2-yl)amino]methyl]-1H-pyrazol-3-yl]-N'-(3,4,6,10b-tetrahydro-2-methyl-6-oxo-2H-[1,3]oxazino[2,3-a]isoindol-10-yl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	9.49	157.85

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.30	-1.30

STN INTERNATIONAL LOGOFF AT 10:34:30 ON 20 SEP 2003